

AMENDMENTS TO THE CLAIMS:

This listing of the claims will replace all prior versions, and listings of claims in the application:

Listing of Claims

20. (Currently Amended) A non-naturally occurring mutant human hemoglobin wherein the leucine residue at position 105 of the  $\beta$ -chains ~~(SEQ ID NO: 7)~~ (SEQ ID NO:8) is replaced by a tryptophan residue.

21. (Original) The hemoglobin of Claim 20 possessing low oxygen affinity as compared to normal human adult hemoglobin.

22. (Original) The hemoglobin of Claim 21 further possessing high cooperativity in oxygen binding comparable to normal human adult hemoglobin.

23. (Original) The hemoglobin of Claim 20 which is produced recombinantly.

24. (Currently Amended) rHb ( $\beta$ L105W) ~~(SEQ ID NO:7)~~  
(SEQ ID NO:8).

25. (Currently amended) An artificial mutant hemoglobin which in a cell-free environment has oxygen binding properties comparable to those of human normal adult hemoglobin in red blood cells wherein said hemoglobin contains a mutation such that the leucine residue at position 105 of the  $\beta$ -chains is tryptophan ~~(SEQ ID NO: 7)~~ (SEQ ID NO: 8).

26. (Original) The hemoglobin of Claim 25 which is produced recombinantly.

27. (Currently Amended) A non-toxic pharmaceutical composition comprising a non-naturally occurring mutant hemoglobin wherein the leucine residue at position 105 of the  $\beta$ -chains is replaced by a tryptophan residue ~~(SEQ ID NO: 7)~~ (SEQ ID NO: 8) in a pharmaceutically acceptable carrier.

28. (Original) The composition of Claim 27 wherein said hemoglobin in a cell-free environment has oxygen binding properties lower than those of human normal adult hemoglobin.

29. (Currently Amended) The composition of Claim 28 wherein said hemoglobin is rHb ( $\beta$ L105W) ~~(SEQ ID NO: 7)~~ (SEQ ID

31. (Currently Amended) A non-naturally occurring low oxygen affinity mutant hemoglobin that has oxygen binding properties comparable to those of human normal adult hemoglobin in the presence of the allosteric effector 2,3-bisphosphoglycerate, wherein the leucine residue at position 105 of each of the  $\beta$ -chains is replaced by a tryptophan residue ~~(SEQ ID NO:7)~~ (SEQ ID NO:8).

32. (Currently Amended) A non-naturally occurring mutant human hemoglobin wherein ~~said hemoglobin contains a mutation of~~ the leucine residue at position 105 of the  $\beta$ -chains ~~(SEQ ID NO:7) possessing~~ is replaced by a tryptophan residue (SEQ ID NO:8), wherein said hemoglobin possesses oxygen-binding properties of oxygen affinity as measured by  $P_{50}$  and cooperativity as measured by the Hill coefficient ( $n_{max}$ ) and similar to those of Hb A in the presence of the allosteric effector 2,3-bisphosphoglycerate as follows:  $P_{50}$  about 28.2 mm Hg,  $n_{max}$  about ~~2.6~~ 2.60 in 0.1 M sodium phosphate at pH 7.4 and 29°C.

36. (Currently Amended) A method of treating a human subject, comprising administering to said subject a nontoxic

SEQ ID NO:8

37. (Currently Amended) rHb ( $\beta$ L105W) (SEQ ID NO:8).  
derived from cells transformed with pHE7004.

38. (New) The hemoglobin of Claim 22 further possessing  
increased stability against autooxidation.